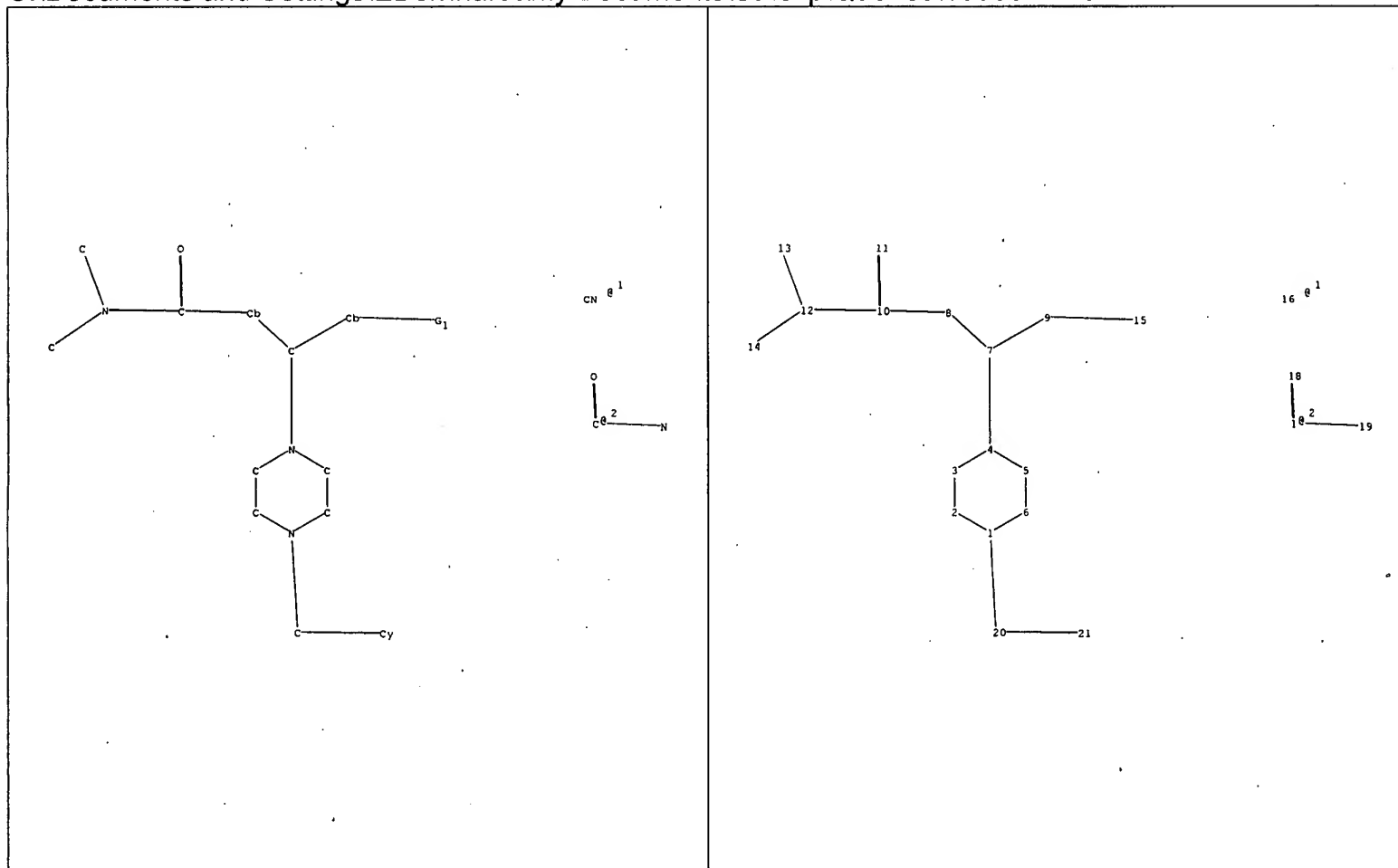


## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L4	454866	(\$3amino)carbonyl near2 phenyl near10 piperazin-1-yl	US-PGPUB; USPAT	OR	OFF	2007/06/23 18:52
L5	4819	((544/360) or (544/363) or (544/369) or (544/370) or (544/372) or (544/379) or (544/396)).CCLS.	US-PGPUB; USPAT	OR	OFF	2007/06/23 18:53
L7	3584	I4 and I5	US-PGPUB; USPAT	OR	OFF	2007/06/23 18:55
L8	1885	I7 and (opioid or sigma or delta)	US-PGPUB; USPAT	OR	OFF	2007/06/23 18:56



chain nodes :

7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

ring nodes :

1 2 3 4 5 6

chain bonds :

1-20 4-7 7-8 7-9 8-10 9-15 10-11 10-12 12-13 12-14 17-18 17-19 20-21

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

1-2 1-6 1-20 2-3 3-4 4-5 4-7 5-6 9-15 10-11 10-12 12-13 12-14 17-18 17-19 20-21

exact bonds :

7-8 7-9 8-10

isolated ring systems :

containing 1 :

G1:[\*1],[\*2]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS8:Atom 9:Atom 10:CLASS11:CLASS12:CLASS13:CLASS14:CLASS15:CLASS16:CLASS17:CLASS18:CLASS19:CLASS20:CLASS21:Atom

Generic attributes :

8:

Saturation : Unsaturated

Number of Carbon Atoms : less than 7

Type of Ring System : Monocyclic

9:

Saturation : Unsaturated

Number of Carbon Atoms : less than 7

Type of Ring System : Monocyclic

21:

Saturation : Unsaturated

10/533744

=> d his

(FILE 'HOME' ENTERED AT 16:03:26 ON 23 JUN 2007)

FILE 'REGISTRY' ENTERED AT 16:03:42 ON 23 JUN 2007

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 17 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 16:04:30 ON 23 JUN 2007

L4 1 S L3

FILE 'CAOLD' ENTERED AT 16:04:59 ON 23 JUN 2007

L5 0 S L3

FILE 'CHEMCATS' ENTERED AT 16:05:09 ON 23 JUN 2007

L6 0 S L3

FILE 'REGISTRY' ENTERED AT 16:05:58 ON 23 JUN 2007

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.45

178.23

FILE 'CAPLUS' ENTERED AT 16:06:29 ON 23 JUN 2007

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FILE LAST UPDATED: 22 Jun 2007 (20070622/ED)

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(FILE 'HOME' ENTERED AT 16:03:26 ON 23 JUN 2007)

FILE 'REGISTRY' ENTERED AT 16:03:42 ON 23 JUN 2007

L1 STRUCTURE UPLOADED

L2 0 S L1

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L4 1 S L3

10/533744

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L6 0 S L3

FILE 'REGISTRY' ENTERED AT 16:05:58 ON 23 JUN 2007

FILE 'CAPLUS' ENTERED AT 16:06:29 ON 23 JUN 2007

=> s l3 bib abs hitstr

MISSING OPERATOR L3 BIB

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s l3

L7 1 L3

=> d l7 bib abs hitstr

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:412930 CAPLUS

DN 140:423707

TI Preparation of 4-(phenylpiperazinylmethyl)benzamides for treatment of pain or gastrointestinal disorders

IN Brown, William; Griffin, Andrew; Plobeck, Niklas; Walpole, Christopher

PA Astrazeneca AB, Swed.

SO PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DT Patent

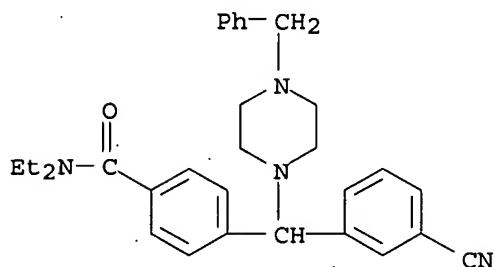
LA English

FAN.CNT 1

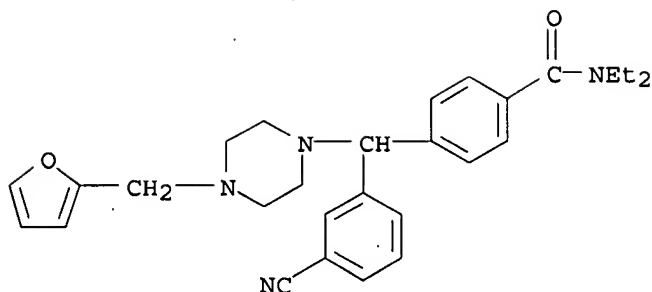
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PI	WO 2004041800	A1	20040521	WO 2003-SE1703	20031105
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	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2502733	A1	20040521	CA 2003-2502733	20031105
	AU 2003274884	A1	20040607	AU 2003-274884	20031105
	EP 1562922	A1	20050817	EP 2003-759164	20031105
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003015998	A	20050920	BR 2003-15998	20031105
	CN 1711251	A	20051221	CN 2003-80102825	20031105
	JP 2006507296	T	20060302	JP 2004-549772	20031105
	US 2006167004	A1	20060727	US 2005-533744	20050504
	NO 2005002699	A	20050606	NO 2005-2699	20050606
PRAI	SE 2002-3300	A	20021107		
	WO 2003-SE1703	W	20031105		
OS	MARPAT 140:423707				
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

- AB Title compds. I [wherein R1 = (un)substituted (hetero)aryl; R2 = H or (un)substituted alkyl, aryl, or heterocyclyl; or pharmaceutically acceptable salts, enantiomers, or mixts. thereof] were prepared as opioid  $\delta$  receptor ligands. For example, 4-carboxybenzaldehyde was amidated with diethylamine using  $\text{SOCl}_2$  in  $\text{CH}_2\text{Cl}_2$  to give N,N-diethyl-4-formylbenzamide (90%). Coupling of the amide with 1-piperazinecarboxylic acid 1,1-dimethylethyl ester in the presence of benzotriazole in toluene, followed by reaction with 3-cyanophenylzinc iodide in THF, afforded 4-[(3-cyanophenyl)[4-[(diethylamino)carbonyl]phenyl]methyl]-1-piperazinecarboxylic acid 1,1-dimethylethyl ester. Deprotection of the piperazine (39%) using TFA in  $\text{CH}_2\text{Cl}_2$  and alkylation (57%) with benzaldehyde in the presence of sodium triacetoxyborohydride in  $\text{CH}_2\text{Cl}_2$  provided 3-[[4-[(diethylamino)carbonyl]phenyl](4-benzylpiperazin-1-yl)methyl]benzonitrile. Conversion of the nitrile to the amide with KOH in t-BuOH and chiral HPLC separation of the enantiomers gave (-)-II (99% optical purity). In binding assays using human 293S cells expressing cloned human opioid receptors and neomycin resistance, (-)-II proved to be an effective  $\delta$  receptor ligand ( $\text{IC}_{50} = 0.26 \text{ nM}$ ) and showed some activity toward the  $\kappa$  ( $\text{IC}_{50} = 112 \text{ nM}$ ) and  $\mu$  ( $\text{IC}_{50} = 7.7 \text{ nM}$ ) receptors. In functional assays, (-)-II demonstrated  $\delta$  receptor agonist activity by activating the binding of GTP to G-proteins. Thus, I and their pharmaceutical compns. are useful in therapy, in particular for the treatment of gastrointestinal disorders or the management of pain (no data).
- IT 691358-45-9P, 3-[[4-[(Diethylamino)carbonyl]phenyl](4-benzylpiperazin-1-yl)methyl]benzonitrile 691358-46-0P, 3-[[4-[(Diethylamino)carbonyl]phenyl][4-(2-furylmethyl)piperazin-1-yl]methyl]benzonitrile  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (intermediate; preparation of (phenylpiperazinylmethyl)benzamides as  $\delta$  receptor agonists for treatment of pain or gastrointestinal disorders)
- RN 691358-45-9 CAPLUS
- CN Benzamide, 4-[(3-cyanophenyl)[4-(phenylmethyl)-1-piperazinyl]methyl]-N,N-diethyl- (9CI) (CA INDEX NAME)



- RN 691358-46-0 CAPLUS
- CN Benzamide, 4-[(3-cyanophenyl)[4-(2-furanylmethyl)-1-piperazinyl]methyl]-N,N-diethyl- (9CI) (CA INDEX NAME)



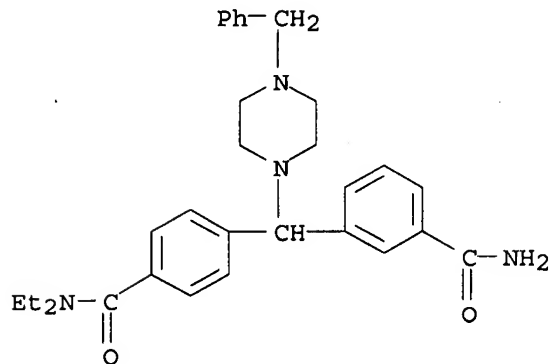
IT 691358-51-7P, 3-[[4-[(Diethylamino)carbonyl]phenyl][4-benzylpiperazin-1-yl]methyl]benzamide 691358-56-2P, 3-[[4-[(Diethylamino)carbonyl]phenyl][4-(2-furylmethyl)piperazin-1-yl]methyl]benzamide 691358-62-0P, 3-[[4-[(Diethylamino)carbonyl]phenyl][4-(phenylmethyl)-1-piperazinyl]methyl]-N-methylbenzamide

RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

( $\delta$  receptor agonist; preparation of (phenylpiperazinylmethyl)benzamide s as  $\delta$  receptor agonists for treatment of pain or gastrointestinal disorders)

RN 691358-51-7 CAPLUS

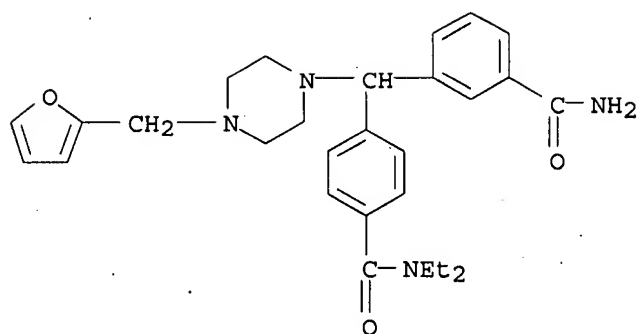
CN Benzamide, 4-[[3-(aminocarbonyl)phenyl][4-(phenylmethyl)-1-piperazinyl]methyl]-N,N-diethyl- (9CI) (CA INDEX NAME)



RN 691358-56-2 CAPLUS

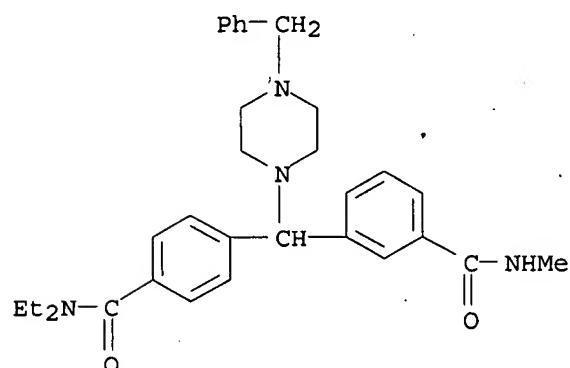
CN Benzamide, 4-[[3-(aminocarbonyl)phenyl][4-(2-furanylmethyl)-1-piperazinyl]methyl]-N,N-diethyl- (9CI) (CA INDEX NAME)

10/533744



RN 691358-62-0 CAPLUS

CN Benzamide, N,N-diethyl-4-[[3-[(methylanino)carbonyl]phenyl][4-(phenylmethyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



IT 691883-84-8P 691883-85-9P 691883-86-0P

691883-87-1P 691883-88-2P 691883-89-3P

RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

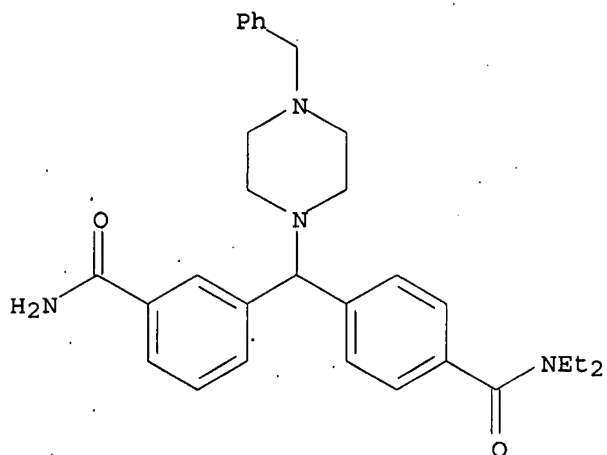
( $\delta$  receptor agonist; preparation of (phenylpiperazinylmethyl)benzamide s as  $\delta$  receptor agonists for treatment of pain or gastrointestinal disorders)

RN 691883-84-8 CAPLUS

CN Benzamide, 4-[[3-(aminocarbonyl)phenyl][4-(phenylmethyl)-1-piperazinyl]methyl]-N,N-diethyl-, hydrochloride (5:16), (-)- (9CI) (CA INDEX NAME)

Rotation (-).

10/533744

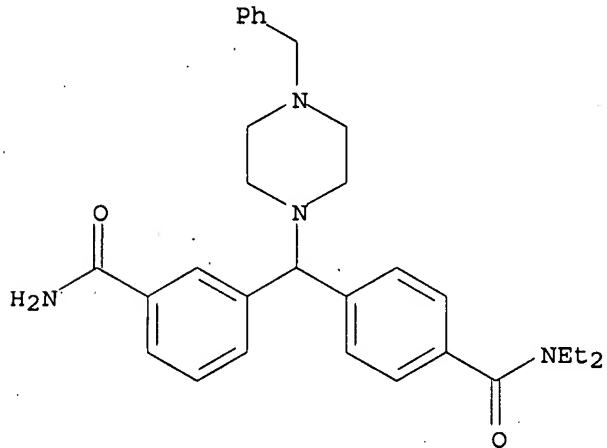


●16/5 HCl

RN 691883-85-9 CAPLUS

CN Benzamide, 4-[[3-(aminocarbonyl)phenyl][4-(phenylmethyl)-1-piperazinyl]methyl]-N,N-diethyl-, hydrochloride (10:31), (+)-(9CI) (CA INDEX NAME)

Rotation (+).



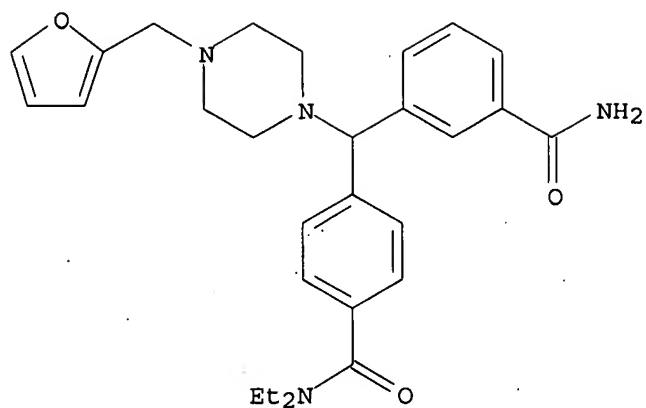
●31/10 HCl

RN 691883-86-0 CAPLUS

CN Benzamide, 4-[[3-(aminocarbonyl)phenyl][4-(2-furanylmethyl)-1-piperazinyl]methyl]-N,N-diethyl-, hydrochloride (5:13), (-)-(9CI) (CA INDEX NAME)

Rotation (-).

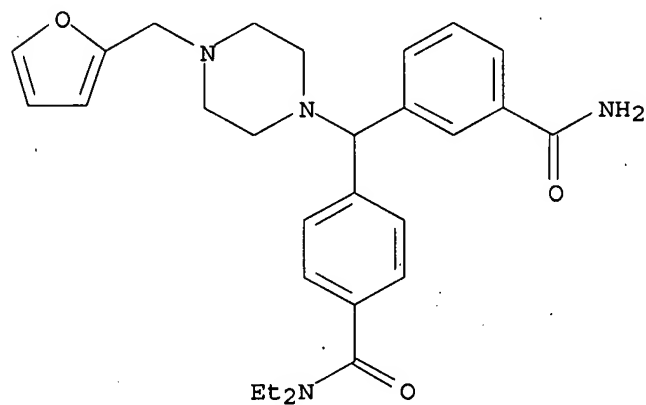
10/533744



●13/5 HCl

RN 691883-87-1 CAPLUS  
CN Benzamide, 4-[[3-(aminocarbonyl)phenyl][4-(2-furanylmethyl)-1-piperazinyl]methyl]-N,N-diethyl-, hydrochloride (10:7), (+)- (9CI) (CA INDEX NAME)

Rotation (+).



●7/10 HCl

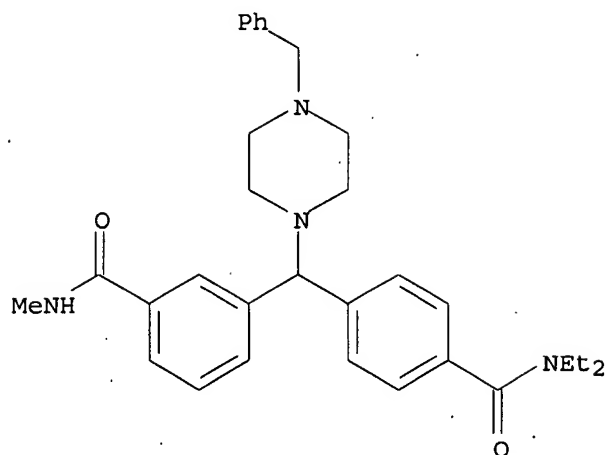
RN 691883-88-2 CAPLUS  
CN Benzamide, N,N-diethyl-4-[[3-[(methylamino)carbonyl]phenyl][4-(phenylmethyl)-1-piperazinyl]methyl]-, (-)-, trifluoroacetate (5:8) (9CI) (CA INDEX NAME)

CM 1

CRN 691358-63-1  
CMF C31 H38 N4 O2

10/533744

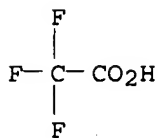
Rotation (-).



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 691883-89-3 CAPLUS

CN Benzamide, N,N-diethyl-4-[[3-[(methylamino)carbonyl]phenyl][4-(phenylmethyl)-1-piperazinyl]methyl]-, (+)-, trifluoroacetate (5:8) (9CI)  
(CA INDEX NAME)

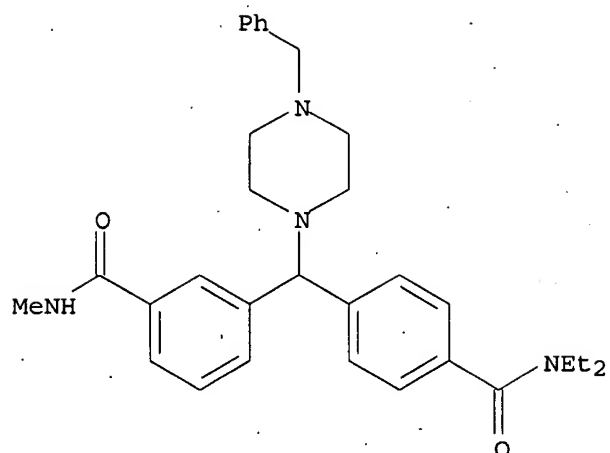
CM 1

CRN 691358-64-2

CMF C31 H38 N4 O2

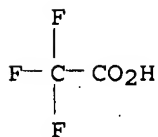
Rotation (+).

10/533744



CM 2

CRN 76-05-1  
CMF C2 H F3 O2



=> log h

COST IN U.S. DOLLARS

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE

ENTRY

5.74

SINCE FILE

ENTRY

-0.78

TOTAL

SESSION

183.97

TOTAL

SESSION

-0.78

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 16:07:07 ON 23 JUN 2007